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John N. German

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ELECTROPHORETIC PATTERNS OF TUMORS OF THE CENTRAL NERVOUS SYSTEM

by

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B. A. Yale University
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A thesis presented to the faculty of the Yale University School of Medicine in candidacy for the Degree of Doctor of Medicine.

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PROJECT

The purpose of this investigation is the study of protein composition of primary and metastatic tumors of the central nervous system, cyst fluid, serum, and cerebrospinal fluid by means of electrophoresis.

HISTORY

In the early bibliography investigators were predominantly concerned with the origin of the cyst fluid. The controversy which evolved from these studies centered around the question of whether the cyst fluids were derived from the serum as transudates, or were secreted from the tumor tissue. In 1939 Stern[1] said of cyst fluid; "The comparatively high amounts of protein which resemble those of inflammatory exudates is explained by the high permeability of pathological vessels and by mesodermal reactive processes. There is no relation between the chemical nature of the fluid on the one hand and the site or histological nature of the cyst on the other."

In a paper concerning the chemical analysis of tumor tissue and cyst fluid, Cumings[2] in 1943 suggested that the fluid was derived from a breakdown of tumor and cerebral tissues. Cumings continued his work on cyst fluids of tumors of the central nervous system, and

in 1950[3] stated: "The results suggest that degeneration of tumour initiates the formation of cerebral cysts followed by some transudation of fluid from blood vessels, except for those cysts formed in association with hemangioblastoma and neurofibroma in which no evidence of necrosis is found."

In 1953 Cumings[4] found, by electrophoresis, a large amount of beta globulin in cyst fluids and cerebrospinal fluids from patients with gliomas and metastatic tumors of the central nervous system. He further found that if these cysts were drained, they quickly refilled with fluid, but at this time the electrophoretic pattern more closely resembled that of the patient's serum. At that time he suggested that the beta globulins of the cyst fluid were derived from the tumor tissue, while the general structure of the electrophoretic pattern was that of the serum. In this study the electrophoretic patterns of the sera generally were within the range of normal, but one case of glioblastoma multiforme showed an increase in the beta globulin segment.

In 1954 Spiegel-Adoff and Wycis[5] stated that enzymatic action was partially responsible for the formation of cyst fluids: "A group of tumors (craniopharyngioma and gliomas) could be differentiated in which cyst formation was associated with definite enzymatic activity against nucleic acids and tigroid bodies, while such an

activity was absent in a cystic acoustic neurinoma. This seems to suggest that various mechanisms may be responsible for cyst formation in tumors, one of which is destruction of cells by enzymatic products originating in the tumor metabolism."

In 1958, A. Spina-Franca[6] studied the electrophoretic patterns of ten cyst fluids and their correlative sera. The results of the cyst fluids are shown in Table I. In this study he found that the protein values of the cyst fluids were similar to those of the sera, with the exception of the meningioma and the craniopharyngioma in which the cyst fluid albumin was lower than that of the serum.

Summarizing the review of the literature, there are diverse opinions expressed on the origin of the cyst fluid; e.g. enzymatic action, serum transudation, necrosis of tumor tissue. The idea of the cyst fluid being secreted by the tumor tissue seems to have lost favor in recent years.

In 1950 Mider, Alling and Morton[7] studied the plasma proteins in patients with neoplastic disease not restricted to the central nervous system. They found a hypoalbuminemia in all cases, even those with small, well localized lesions. The total globulin content was increased, particularly in the alpha globulin segment. In general, they found the more extensive the neoplasm, the more abnormal the distribution of proteins. Snell and Gross,[8] in a

TABLE I

RESULTS OF ELECTROPHORETIC PATTERNS OF CYST FLUIDS FROM A. SPINA - FRANCA

CASE	CYST FLUID	ALBUMIN %	ALPHA-1%	ALPHA-2%	BETA %	GAMMA %
1	Astrocytoma	68.0	2.6	2.7	12.2	14.5
2	Astrocytoma	59.0	2.1	4.0	9.4	25.5
3	Astrocytoma	65.5	2.0	4.0	12.0	16.5
4	Astrocytoma	65.0	2.0	3.6	13.0	16.4
5	Astrocytoma	68.0	2.6	6.0	10.4	13.0
6	Astrocytoma	61.0	1.5	5.0	14.0	18.5
7	Ependymoma	63.0	3.0	6.0	12.0	16.0
8	Meningioma	54.0	2.9	6.2	18.1	18.8
9	Craniopharyngioma	45.0	3.0	7.3	19.0	25.7
10	Craniopharyngioma	46.0	4.3	9.2	10.5	30.0

carefully controlled study in 1956 noted similar results in the albumin segment, but felt that the changes in the globulin components were not statistically significant.

Robez, Hess and Forster[9] in 1955 studied the serum proteins in patients with malignant and benign neoplasms of the central nervous system, and also of patients with malignant neoplasms of other organs, (mouth, lung, and cervix). The results are shown in Table II. Of note is the striking similarity of the protein fractions in each of the three categories, and the consistantly low serum albumin.

Concerning the protein composition of brain and tumor tissue, Kruwczynski, Drewnowska, Fleszynski and Ryeaj[10] in 1958 found that the blood-brain passage of protein is very slow; further, they expressed the opinion that brain tissue turns over protein at a relatively slow rate when compared with other visceral organs. Richter[11] in 1959 found that the protein content of brain varies from structure to structure, being higher in those regions which mature earliest. Cipriani, Missere, Alvisi and Tonini[12] in 1958 studied the electrophoretic patterns of normal rat brain and human tumors of the central nervous system. They found that tumors of glial origin produce patterns similar to that of the normal rat brain, while a meningioma produced a different type of pattern; consisting

TABLE II

AVERAGE RESULTS OF ELECTROPHORETIC PATTERNS OF SERUM FORM PATIENTS WITH NEOPLASTIC DISEASE

FROM ROBEZ, HESS AND FORSTER

NEOPLASM	ALBUMIN %	ALPHA-1%	ALPHA-2%	BETA %	GAMMA %
Malignant tumors-central nervous system-10 cases	37.5±6.3	6.5±2.8	16.5±4.1	15.7±4.1	22.4±6.5
Benign tumors-central nervous system-6 cases	38.3±6.4	5.0±2.1	13.7±5.8	16.3±6.7	26.6±5.8
Malignant tumors-other organs-7 cases	38.6±5.7	7.2±2.4	15.1±4.0	14.0±3.5	25.1±2.8

of a higher albumin fraction. While our study was in progress, these same investigators[13,14] in 1958 and 1957 studied the electrophoretic patterns of tumor tissue, cyst fluid and serum from patients with neoplasms of the central nervous system. Unfortunately, the study was limited to a small number of cases, the results of which are found in Table III. Three oligodendrogliomas, one astrocytoma, one glioblastoma and two ependymomas were evaluated. In this series there is generally a correlation between the cyst fluids and the sera; the tumor tissue generally showing a lower albumin and a high alpha and beta globulin.

In 1960, Goldstein, Hill, McKenzie, McGuckin and Svien[15] studied by electrophoresis the protein, glycoprotein and lipoprotein in cerebrospinal fluid and published a set of normal values for cerebrospinal fluid and serum. (See Table IV). This study also led to some interesting findings in the cerebrospinal fluid of patients with intracranial tumors: "In patients with tumors of the central nervous system, the electrophoretic pattern of the proteins of the lumbar cerebrospinal fluid was within normal range until high concentrations of protein appeared. In some patients with brain tumor in whom the total protein content of the lumbar fluid was in the range of 100 to 400 mg. per 100 ml., there was some increase in the concentration of the alpha-2 globulin and gamma globulin.

TABLE III

ELECTROPHORETIC PATTERN RESULTS FORM CIPRIANI, MISSERE, ALVISI AND TONINI

NEOPLASM	MATERIAL	X	ALBUMIN	ALPHA	BETA	Y	GAMMA
Oligodendroglioma	Tumor	5.42	7.48	33.93	40.30		14.84
	Cyst		59.84	13.82	8.23		17.98
	Serum		44.67	18.60	15.47		21.24
	Tumor	3.85	6.45	22.66	43.32		26.62
	Cyst		46.09	15.30	12.35		26.23
	Serum		43.27	20.69	13.14		22.92
	Tumor	4.50	9.27	15.34	34.38		36.48
	Cyst		17.10	40.78	17.93		24.11
	Serum		42.21	17.91	13.22		25.53
Astrocytoma	Tumor		22.29	24.90	19.78		32.35
	Cyst		41.54	15.20	10.28		32.93
	Serum		41.15	22.18	17.33		19.33
Glioblastoma	Tumor		31.41	13.13	26.81		28.56
	Cyst		48.28	15.17	15.56	5.58	15.38
Ependymoma	Cyst		36.05	22.10	13.42	5.04	22.36
	Serum		38.48	17.23	14.81		29.46
	Cyst		34.73	20.61	15.57		28.91
	Vent. Fl.	16.89	28.58	13.30	17.43		23.77
	C.S.F.	8.38	32.85	19,80	22.13		16.81

TABLE IV

RANGE OF NORMAL FOR CEREBROSPINAL FLUID AND SERUM ELECTROPHORESIS ACCORDING TO GOLDSTEIN, HILL, McKENZIE, McGUCKIN AND SVIEN

MATERIAL	CASES	X	ALBUMIN	ALPHA-1	ALPHA-2	BETA	GAMMA
Serum	80	--------	56.0±3.1	4.9±0.56	9.5±1.2	12.1±1.4	17.5±2.7
C.S.F.	21	4.6±1.3	49.5±6.5	6.7±2.0	8.3±2.1	18.5±4.8	11.2±2.7

In some of the patients with intracranial astrocytoma, the lumbar fluid contained increased amounts of alpha-1 and gamma glycoprotein associated with a high concentration of total protein and increased concentration of total glycoprotein.

'In six patients with brain tumor and an increased concentration of total protein in the lumbar cerebrospinal fluid, a lipoprotein was found in the lumbar fluid. In each patient, the lipoprotein was in the alpha-2 globulin position. In four of the six patients, the alpha-2 globulin component in the lumbar fluid was also increased."

In 1961, Szliwowski and Cumings[16] found a correlation between the total protein content of cyst fluid and the degree of malignancy of astrocytoma, but they did not study the electrophoretic patterns of these fluids. (See Table V)

TABLE V

Cerebral Astrocytoma	Grade 1	Grade 2	Grade 3	Grade 4
Total protein (gm./100ml.)	3+	3.5+	4+	4.0-6.0

In summary, from these studies we see that there is a definite change in the serum protein electrophoretic patterns of patients with malignant neoplastic disease of any organ system. The most general finding being that of hypoalbuminemia. There appears

to be little difference in the serum protein fractions in cases of benign and malignant neoplasms of the central nervous system by comparison with patients with tumors of other organs.[9] It has been demonstrated that the protein composition of the cyst fluid found in tumors of the central nervous system is closely related to that of the serum.[2,3,4]

MATERIALS AND METHOD

The electrophoretic patterns of tumor tissue, cyst fluid, serum and/or cerebrospinal fluid from seventy-two patients with lesions of the central nervous system were used in this study. In addition, samples of normal brain, kidney and spleen were used as controls. These specimens were obtained from either the operating room or the autopsy room of the Grace-New Haven Community Hospital, The Hartford Hospital or the New London Hospital.

The materials used in this experiment consisted of:

Tumor tissue	48 samples	10 tumor types
Cyst fluid	18 samples	8 tumor types
Serum	12 samples	8 tumor types
Cerebrospinal fluid	5 samples	4 tumor types

Each specimen was kept sterile and maintained at -20 degrees C. until such time was available for its evaluation. Upon thawing, each specimen was cut into 0.5 cm. cubes and washed twice with sterile normal saline to remove the remnants of blood. The washed tissue was then homogenized in a 10 ml. hand homogenizer, with normal saline, to form a protein suspension. The suspension was quickly frozen to -70 degrees C. and rethawed to +30 degrees C. twice over to break up any remaining cells. The resultant suspension was centrifuged at 1500 r.p.m. for ten minutes to remove any remnants of tissue. The supernatent fluid was then applied to the electrophoretic strips in amounts varying from 0.02 to 0.05 ml., depending on the estimated protein concentration of the fluid.

The cyst fluids were applied directly to the filter paper electrophoretic strips in amounts varying from 0.01 to 0.05 ml. in accordance with the estimated protein concentration of the fluid. The serum samples were applied to the electrophoretic strips in amounts of 0.01 ml.

The method of filter paper electrophoresis, such as that used in this experiment, was first described by Wieland and Fischer in 1948[17] and by Cremer and Tiselius in 1950.[18]

Specifically, the technique of electrophoresis used in our study, was that of the Spinco division of the Beckman company: Filter paper

strips were placed in a cell containing Veronal buffer, (pH=8.6, 2.61 gm. diehtyl barbituric acid, 4.6 gm. sodium diethyl barbituric acid in one liter of distilled water). An electric current of 7.5 milliamperes per cell, (eight paper strips) was run for a period of sixteen hours. The strips were then removed from the cell and placed in a hot air oven at 100 degrees C. for thirty minutes. In this manner the protein was fixed to the paper. The strips were then stained with Bromphenol Blue dye for six hours. (0.1 gm. bromphenol blue, 50 mg. zinc sulfate in enough 95% ethanol to dissolve the dye, 50 ml. of glacial acetic acid and made up to one liter with distilled water.) The strips were then washed for a total of twelve minutes in a solution containing 50 ml. of glacial acetic acid and 950 ml. of distilled water. Fixation of the dye was carried out with a solution consisting of 9 gm. of sodium acetate, 100 ml. of glacial acetic acid and 900 ml. of distilled water. This process required six minutes. The strips were then damp-dried on blotter paper for fifteen minutes and then were placed in ammonia vapor for six minutes. After drying in air overnight the strips were read on a Spinco Analytrol, which indicates the percentage of each protein segment. All comparisons of protein values are in relation to normal human serum unless otherwise indicated. The standard values of normal serum in

the Grace-New Haven Community Hospital (Dr. Klatskin's laboratory) read as follows:

ALBUMIN	ALPHA-1	ALPHA-2	BETA	GAMMA
46.5-73.7%	1.7-6.5%	4.2-13.4%	6.4-17.2%	7.3-22.9%

RESULTS

The protein values of the control material (brain, kidney, spleen) will be presented first, followed by tumor, cyst fluid, serum and cerebrospinal fluid.

Brain: (Table VI and Chart 1) The patterns from eleven samples of normal adult brain showed an elevation in the beta and gamma globulin components and very low albumin. Of note, were two samples of fetal brain which showed unusual electrophoretic patterns, particularly in relation to the elevated alpha-2 globulin.

Kidney: (Table VII and Chart 2) In this tissue both the beta and gamma globulin segments were found to be elevated, the beta segment exceeding the gamma. The albumin was found to be markedly decreased.

Spleen: (Table VIII and Chart 3) Of particular interest in this tissue was the extreem elevation of the beta globulin component. But, it is known that hemoglobin migrates with the beta globulin

component of serum, and the homogenized spleen certainly would contain a large amount of hemoglobin. The albumin and alpha-1 and alpha-2 globulins were markedly reduced.

Tumor tissue: (Table IX) In all types of tumor studied, the electrophoretic pattern showed an elevation of the beta and gamma globulin segments above that of normal serum. In addition, it was noted that the albumin segments were considerably lower than those of normal serum, regardless of the degree of malignancy or the origin of the tumor.

Cyst fluid: (Table X) In general, the cyst fluids studied followed a constant pattern: the beta and gamma globulins were elevated or just above the upper range of normal for serum. Again, the albumin segment was depressed or just below the lower range of normal for serum. But, the cyst fluids did not vary from the normal serum values to the extreem degrees as did the tumor tissue homogenates.

Serum: (Table XI) In the sera studied, the gamma globulin segments ran consistantly in the range of normal, but alpha-1, alpha-2 and beta segments ran consistantly above, or on the upper side of the normal range. The albumin segments of these patterns were on the lower side of normal serum values.

Cerebrospinal fluid: (Table XII) An elevation in the beta and gamma globulin and a slight decrease in the albumin segment were commonly seen in this material.

The electrophoretic patterns are now grouped according to the histopathological diagnosis of the examined tumors.

GLIOBLASTOMA MULTIFORME

Tumor tissue	16 cases
Cyst fluid	4 cases
Serum	4 cases
Cerebrospinal fluid	2 cases

The tumor tissue (Chart 4) showed a marked increase in the beta and gamma globulin segments. In no case was the beta globulin segment lower than the upper range of the normal serum. On the other hand, the pattern of the cyst fluids (Chart 5) and the sera (Chart 6) showed a normal gamma globulin, an increase in the beta and alpha-2 segments and a decrease in the albumin segment. The two charts (5 and 6) were almost identical in their deviation from normal. The results of the cerebrospinal fluid (Table XII) again showed the increase in the beta and gamma globulin segments and a decrease in the albumin segment, but the deviations from normal were greater than those of the cyst fluid or serum.

ASTROCYTOMA

Tumor tissue	3 cases
Cyst fluid	3 cases
Serum	1 case
Cerebrospinal fluid	none available

The electrophoretic patterns of the tumor tissue homogenates (Chart 7) showed a low albumin segment and an elevation of the alpha-1, beta, and gamma globulin segments. The cyst fluid of these tumors (Chart 8) showed an increase only in the beta globulin segment, while the serum, (Table XI) revealed a decrease in the albumin and an increase in the alpha-1 and alpha-2 globulin segments, but a normal beta globulin.

METASTATIC CARCINOMA

Tumor tissue	8 cases
Cyst fluid	2 cases
Serum	1 case
Cerebrospinal fluid	none available

The tissue homogenates of these tumors (Chart 9) produced patterns with increased gamma globulins and, most particularly, quite high beta globulins. The albumin segment was again low. The cyst fluid, (Table X) and serum (Table XI) revealed patterns within the range of normal, with the exception of an elevation in

the beta globulin segment of the serum.

MENINGIOMA

Tumor tissue	11 cases
Cyst fluid	2 cases
Serum	1 case
Cerebrospinal fluid	none available

The meningioma tumor tissue patterns (Chart 10) showed high beta and gamma globulin segments and a low albumin segment. The cyst fluid (Table X) and the serum (Table XI) were normal with the exception of an increase in the alpha-2 globulin segment of the serum.

ACOUSTIC NEURINOMA

Tumor tissue	3 cases
Cyst fluid	none available
Serum	none available
Cerebrospinal fluid	1 case

The tumor tissue electrophoretic patterns (Chart 11) revealed an increase in the beta globulin segment and a low albumin; the gamma globulin segment was within the range of normal. The cerebrospinal fluid (Table XII) reflected this same pattern, with a slight increase in the beta globulin.

OLIGODENDROGLIOMA

Tumor tissue.......................2 cases

Cyst fluid..........................1 case

Serum...............................1 case

Cerebrospinal fluid.................none available

The tissue from these tumors (Table IX) revealed a markedly high beta globulin, a high gamma globulin and a very low albumin. The cyst fluid (Table X) fell into the range of normal, while the serum (Table XI) reflected the high beta globulin and low albumin of the tumor tissue.

PITUITARY ADENOMA

Tumor tissue..................2 cases

Cyst fluid.....................1 case

Serum.........................1 case

Cerebrospinal fluid...........none available

Pituitary tumor tissue (Table IX) revealed a strikingly high beta globulin segment, an increased gamma globulin segment and a very low albumin segment. The cyst fluid (Table X) revealed a very high beta globulin segment and a low albumin segment. The serum (Table XI) on the other hand, was within the range of normal.

EPENDYMOBLASTOMA

Tumor tissue........................1 case

Cyst fluid..........................none available

Serum...............................none available

Cerebrospinal fluid.................none available

The electrophoretic pattern of the tumor (Table IX) showed a low albumin segment and an elevation in the alpha-2, beta and gamma globulins. Of note was the presence of the pre-albumin segment of the pattern.

NEUROFIBROMA

Tumor tissue........................1 case

Cyst fluid..........................1 case

Serum...............................1 case

Cerebrospinal fluid.................none available

This tumor presented a pattern (Table IX) with increased alpha-1 and beta globulins and a decrease in the albumin segment. The cyst fluid (Table X) reflected this pattern, while the serum (Table XI) showed a low albumin, high alpha-1 and alpha-2 globulins, but a normal beta globulin segment.

NEUROBLASTOMA

Tumor tissue........................1 case

Cyst fluid..........................none available

Serum...............................none available

Cerebrospinal fluid.................none available

The electrophoretic pattern of this tumor (Table IX) showed an absence of the albumin and alpha-1 globulin, normal alpha-2 globulin and markedly increased beta and gamma globulin segments.

CRANIOPHARYNGIOMA

Tumor tissue......................none available

Cyst fluid........................4 cases

Serum.............................1 case

Cerebrospinal fluid...............1 case

The cyst fluids from these tumors (Chart 12) were very close to the pattern of normal serum. They revealed an elevation in the beta globulin segment only. The serum (Table XI) showed a low albumin and an elevated alpha-2 globulin, while the cerebrospinal fluid (Table XII) revealed a low albumin and a high beta globulin.

SARCOMA

Tumor tissue..............none available

Cyst fluid................none available

Serum.....................none available

Cerebrospinal fluid........1 case

The cerebrospinal fluid from this tumor (Table XII) revealed an albumin just below the range of normal and an alpha-2 globulin markedly elevated.

DISCUSSION

In the electrophoretic analysis of primary and metastatic tumor tissue, high beta and gamma globulin segments were generally found. On the other hand, the albumin segments of these tissues were very low. In general these protein values are similar to those found by Cipriani et al.[13] One series studied by these investigators consisted of but five samples of tumor tissue, with no control material. In another series, rat brain, rather than human brain, was used as the control. No other mention of brain tumor tissue electrophoresis is found in the literature.

In patients with primary and metastatic intracranial neoplasms, the serum was within the range of normal in some cases. But, in three out of four cases of glioblastoma, one case of oligodendroglioma and one case of metastatic carcinoma, an elevation of the beta globulin segment was found, and in seven of the eleven sera studied, a hypoalbuminemia was present. These findings agree with those of Mider et al,[7] who found a hypoalbuminemia in the sera of

many patients with neoplastic disease. They also found an increase in the globulin components, but in the alpha globulin fraction rather than in the beta globulin fraction, as found in our study. Others, Snell and Gross,[8] do not feel that these globulin findings are significant.

The cyst fluid from these tumors contained a combination of these factors, showing an almost normal albumin, and an increase in the beta and gamma globulin segments over those of the serum. Cumings[4] found the albumin content of cyst fluid to be low when compared with normal serum, and the globulin, especially the beta globulin fraction, to be elevated. The cyst fluid protein values of Cipriani et al[13] show such variation that comparison is not possible.

When compared with normal serum protein values, the cerebrospinal fluid of our patients showed a low albumin in all cases, and an increase in beta globulin in three out of five cases. The total protein was much lower in the cerebrospinal fluid than in the cyst fluid. Cumings[4] found that the protein patterns of cerebrospinal fluid, particularly when a malignant tumor of the central nervous system was present, differed markedly from the patterns of the sera. Here, as in the cyst fluid, he found an increase in the beta globulin segment over the normal values of serum.

The examination of normal brain tissue revealed that its gross protein structure is remarkably similar to that of the tumor tissue. By comparison with normal brain tissue homogenate, in the tumor homogenate, almost without exception, the level of the beta globulin component exceeded that of the gamma globulin. In the meningiomas and glioblastomas these values were almost equal. On the other hand, in the normal brain tissue homogenates it was found that the gamma globulins exceeded the beta globulins in seventy percent of the cases, and the average of the gamma globulins was nine percentile points higher than that of the beta globulins. Generally, there was less albumin and alpha-1 globulin found in the brain tissue than in the tumor tissue.

The two samples of fetal brain tissue which were investigated in this experiment were indeed interesting. Sample 2, that of a three months premature infant, showed an elevation of the alpha-2 and gamma globulin segments and a depression in the beta globulin segment. Sample 11, that of a six weeks premature infant, showed an increase in the alpha-1 and beta globulin segments, and a decrease in the alpha-2 and gamma globulin segments when compared to its younger partner. When compared to normal brain tissue, both samples showed an increase in the alpha-1 and alpha-2 globulin segments. Nothing can be said of these findings at the present time,

but further electrophoretic studies of fetal brain tissue in various developmental stages would indeed be interesting at a future date. It is of interest to note that the glioblastoma electrophoretic patterns are more closely related to those of normal brain than to those of the fetal brain.

Eight samples of kidney tissue and seven samples of spleen tissue were examined as controls in this experiment. The albumin in these two tissues, as that of the brain tissue, was very low. Both the alpha-1 and alpha-2 globulins were decreased or on the lower side of normal for human serum. In contrast to this, the alpha-2 globulin segment of the brain tissue was well within the range of normal. The obvious differences in these tissues were found in the beta and gamma globulin segments. In brain, the gamma globulin was about nine percentile points higher than the beta globulin; gamma=47.4, beta=38.6. In the kidney tissue, the picture was reversed, with the gamma globulin being seven percentile points below the beta globulin; gamma=41.6, beta=48.6. The spleen tissues produced an extremely different electrophoretic pattern, showing a beta globulin which was sixty percentile points above the gamma globulin; gamma=17.6, beta=77.2. As previously mentioned, this extreme beta globulin peak can probably be explained on the basis of a high concentration of hemoglobin in the spleen tissue.

No mention of the electrophoretic analysis of these normal tissues can be found in the literature.

The results are now evaluated and compared in relation to the histopathological diagnosis of the tumor.

Tumors of glial origin: (Glioblastoma, Astrocytoma and Oligodendroglioma) The electrophoretic patterns of these tumors were not closely related to each other or to the pattern of normal brain. All three tumors, as well as normal brain tissue, did show a decrease in the albumin component, but the tumors generally had a slightly higher value. With the exception of the astrocytoma, all these tissues had an average alpha-1 value within the range of normal for serum. The astrocytoma showed an alpha-1 globulin of twice the value of the other gliomas. The averages of the alpha-2 globulins in all cases were very close and within the range of normal for serum. Unfortunately, our alpha-1 and alpha-2 values cannot be compared with those of Cipriani et al[13] as their alpha-1 and alpha-2 segments were considered as one value. The averages of the beta globulin components in our series for brain, glioblastoma and astrocytoma were remarkably close, (38.6, 38.4 and 41.6 respectively). But, that of the oligodendroglioma was about ten percentile points higher, and all of these exceeded the value of normal serum. In the work of Cipriani et al,[13] the beta globulin segment of the oligodendroglioma

exceeded those of the astrocytoma and glioblastoma by at least eight percentile points. On the other hand, the gamma globulin average values in our series of the astrocytoma and oligodendroglioma were similar, (30.2 and 30.9 respectively) while that of the glioblastoma was about nine percentile points higher. The brain tissue here was higher still (47.4). This is not varified by Cipriani et al.[13] Thus, in the present study , if one considers the brain tissue electrophoretic pattern as a norm, the astrocytoma is elevated in the alpha-1 globulin segment, the oligodendroglioma is elevated in the beta globulin segment and the glioblastoma is elevated above the other two tumors in the gamma globulin segment.

The examination of the cyst fluids of the gliomas revealed a marked similarity to the pattern of normal serum. Only the glioblastoma, which showed a slight decrease in the albumin and a slight increase in the alpha-1 globulin component, varied from this range of normal for serum.

The work of Cipriani et al,[13] showed a decreased albumin in two out of five cases and an increased gamma globulin in three out of five cases. From these few cases, one could find support for the theory that the cyst fluid is derived from the serum. When the sera of patients with these tumors were studied, a hypoalbuminemia was found in five out of six cases, accompanied by

occasional slight increases in the alpha-1, alpha-2 or beta globulins. This hypoalbuminemia, as previously mentioned,[7] is commonly seen in patients with neoplastic disease, regardless of the origin or the site of the lesion.

In only one of the gliomas, the glioblastoma, were there samples of cerebrospinal fluid studied. These two samples were so completely different that no conclusions could be drawn from them.

Meningioma, Acoustic Neurinoma and Neurofibroma: The tumor tissues of the meningiomas demonstrated a surprising similarity to the electrophoretic patterns of the glioblastoma. Both the acoustic neurinoma and the neurofibroma produced patterns with very low albumin and very high beta globulins, when compared with normal serum. In these tumors the beta globulin segments were ten to thirty percentile points above the gamma globulin components. These patterns were in marked contrast to the meningioma which showed almost equal average beta and gamma globulin values. But, these two tumors also vary greatly in their electrophoretic patterns, for, in the neurofibroma an alpha-1 peak was found, while the average of this protein component was in the range of normal serum in the acoustic neurinoma. No evidence of work on the electrophoresis of these tumors is found in the literature.

The cerebrospinal fluid of the acoustic neurinoma reflected the high beta globulins of the tissue homogenate. Unfortunately there were no other spinal fluid samples received on these particular tumor types. The serum and the cyst fluid of the neurofibroma were similar in that they generally approached the normal range of values for serum and that they both exhibited hypoalbuminemia and a high alpha-1 globulin component. This was the first neoplasm in which any obvious change in the alpha-1 globulin was found, indicating that it might be of interest to study the sera of patients with von Recklinghause's disease in regard to this protein component. In the case of the meningioma, no correlation of the serum, "cyst fluid" (probably a loculation of cerebrospinal fluid) and tumor was found.

Tumors metastatic to the central nervous system: The general pattern produced by these tumors varied from that of normal brain tissue in a manner similar to the oligodendroglioma and the astrocytoma. That is, the average of the beta globulin segment was ten percentile points higher than the average of the gamma globulin. Those patterns produced by the normal spleen and kidney tissues both showed evidence of this increased beta globulin segment. When compared to normal brain, there was nothing unusual in either the albumin or the alpha-2 globulin segments of these tumors, but a slight increase in alpha-1 was noted. Specific protein values of metastatic tumors are not found in the literature.

Two samples of cyst fluid from these tumors produced patterns well within the range of normal for serum. On the other hand, a sample of serum taken from one of these patients produced a pattern with a markedly elevated beta globulin and a slight depression in the alpha-2 globulin. This increase of the beta globulin segment of the serum electrophoretic pattern was also seen in three out of four cases of glioblastoma and in one case with an oligodendroglioma. None of the other serum samples produced this type of pattern, but an elevation in this segment or the alpha segment has been seen in patients with neoplastic disease.[7,9]

Tumors related to the pituitary gland: (Pituitary Adenoma and Craniopharyngioma) The electrophoretic patterns from material collected on these two tumors were in no way related. Regarding the pituitary adenoma, in 1958 Bakey[19] noted an elevation in the cerebrospinal fluid protein from patients with this tumor only when it was found that the growth had exceeded the limits of the sella turcica. This protein elevation returned to normal after the removal of the tumor. In this study there was no chance to confirm this finding as no samples of cerebrospinal fluid were received. Both the tissues and cyst fluid taken from patients with this tumor revealed the highest beta globulin components recorded in this study. This is of particular interest as the serum from one patient produced a

normal pattern, with no indication of an increase in the beta globulin. In this particular case it would appear that the cyst fluid was derived from the tumor and not as a transudate of the serum.

In the case of the craniopharyngioma no consistant trend was detectable. The cyst fluids showed patterns almost within the range of normal for serum, while the cerebrospinal fluid revealed a low albumin and a marked increase in the beta globulin component. A very slight elevation in this component, which was found in the cyst fluid, certainly does not appear to be enough to explain the marked elevation.

Tumors arising from the ependyma: Ependymoblastoma; This tumor showed the usual pattern of the elevated beta and gamma globulin segments and a low albumin, but, in addition it revealed the presence of the X fraction, or pre-albumin. This is a protein fraction which normally migrates at a faster rate than the albumin and is occasionally seen in cerebrospinal fluid. In 1958, Fishman, Rausohoff and Osserman[20] found that ventricular fluid usually contains more of this protein than does the lumbar fluid. Considering this fact and that this particular tumor was derived from the cells lining the lateral ventricle, it is not surprising that this protein should be present in the determination. As far as the remainder of the pattern is concerned, the beta globulin component exceeded the

gamma globulin component by eight percentile points. The alpha-2 globulin component was also found to be markedly elevated, a finding not previously seen.

Neuroblastoma: Unfortunately only one sample of this rare tumor was received, but it revealed a very high beta globulin (56.5), twenty-six percentile points above the gamma globulin component. It also revealed an increase in the alpha-2 globulin, which differentiates it from the pituitary adenoma.

Only one sample of cerebrospinal fluid was received from a sarcoma case. This sarcoma was said to be of meningeal origin. The sample revealed a marked elevation in the alpha-1 globulin segment of the electrophoretic pattern.

In general, this study indicates that there is a difference in the protein composition of various tumors of the central nervous system. In the electrophoretic patterns the following variations from normal brain tissue were found. (Table XIII)

Albumin: When compared with normal brain, the tumor tissue showed an increase in four (astrocytoma, meningioma, ependymoblastoma and neurofibroma) out of ten types, a decrease in one (neuroblastoma), while five were normal. All tumor tissue samples, as well as the normal brain, were markedly below the range of normal for serum. In general, the sera studied showed a

hypoalbuminemia, particularly in the cases of glioblastoma. The cyst fluids usually showed albumin within the range of normal for serum. It was decreased in the cases of glioblastoma, pituitary adenoma and neurofibroma.

Alpha-1 globulin: Five (astrocytoma, metastatic, meningioma, acoustic neurinoma and neurofibroma) out of ten tumors showed an elevation in this segment when compared to normal brain. The neurofibroma tissue showed a marked increase in this segment. Two tumors (pituitary adenoma and neuroblastoma) showed a decrease in this component. Generally, the normal brain revealed alpha-1 values similar to those of normal sera. Two samples of cyst fluid showed an elevation of this segment, the glioblastoma and neurofibroma. This pattern was repeated in the sera of patients with these tumors, as well as in a case of astrocytoma.

Alpha-2 globulin: Using normal brain as a standard, four tumors (glioblastoma, oligodendroglioma, ependymoblastoma and neuroblastoma) showed a slight increase in this segment, while the pituitary adenoma showed a decrease. The range of values found in the tumors were very similar to those of normal sera. Only the cyst fluid from a pituitary adenoma varied from the range of normal for alpha-2 in human serum. This fluid showed a decrease, as did the tumor tissue. Four samples of serum showed an increase in this globulin segment.

Beta globulin: The acoustic neurinoma, pituitary adenoma and neuroblastoma showed marked increases in the globulin component above the values of normal brain. The oligodendroglioma showed a definite increase, but not as striking. No tumor tissue produced beta globulin values below those of normal brain. The cyst fluids of pituitary adenoma, neurofibroma and craniopharyngioma exceeded the values of normal sera. Three out of four cases of glioblastoma, as well as a metastatic carcinoma case and an oligodendroglioma case revealed an increase in the beta globulin segment of the serum.

Gamma globulin: All cases of tumor tissue showed a definite reduction in gamma globulin when compared to normal brain. This indicates a general increase in the mobility of the proteins of the tumor tissue. The sera and cyst fluid were all within the range of normal for human serum.

Pre-albumin: This segment made its appearance once in the series of tumors, that was in an ependymoblastoma growing in the wall of the lateral ventricle.

The definition of electrophoresis[21] indicates that the nature and the free charges on the surface of a particle determines the speed and direction of its migration in an electric field. Of particular interest in this study is the "nature" of the protein; that is, the size, shape, molecular weight and substances with which it is bound, as

well as the surface charges. When all these things are taken into consideration it becomes evident that what is being measured in any particular electrophoretic peak is really far from a pure substance. Two proteins of the same weight may well migrate to a different peak because of a difference in shape, the pH of the buffer solution, or because one is bound to a lipid or a polysaccharide. When these things are taken into consideration, it is not at all surprising to see the marked similarity between the glioblastoma and meningioma tumor tissue homogenate electrophoretic patterns. Alike, though the general patterns are,the chemical structure of the proteins may be very different. Also, in the interpretation of these electrophoretic patterns, one should keep in mind that the tumor tissue specimen contain some normal structures, e.g. neurons, vessels, etc.

During this study a few samples of tumor homogenate were stained (Oil Red-O) for lipid content, rather than protein content. These samples showed that the lipids were primarily in the beta and gamma globulin segments of the pattern. This finding may well indicate that the mass of protein noted in these two globulin components of the tumor tissue patterns is actually lipoprotein in nature. Considering that both the weight and size of a protein particle in part determine its speed of migration, it is understandable why the lipids should be found in those slowly migrating segments. The

lipid part of the complex would certainly increase the weight of the molecule without participating in the character of its charge.

Various methods of treatment given to a patient for a particular lesion may well change the character of the electrophoretic pattern of the specimen. For example, while collecting this group of tumors, I received at different times, three samples of glioblastoma multiforme from one patient (Case 56). The first sample was received from the initial operation, when the diagnosis was made. This sample showed the typical ""neoplastic pattern"" of glioblastoma. The second sample was received approximately six months later from a decompressive procedure after the patient had been treated by neutron capture. The pattern from this sample was unreadable as the proteins did not migrate from the point of application, a finding typical of denatured protein. Three months later the third sample was taken at a further decompressive procedure, after Thio-Teppa perfusion. This sample showed increase in migratory capacity, but still short of that of the first sample. This might be taken to indicate a partial regrowth of this particular part of the tumor, but also the presence of some denatured protein material.

Of the neoplasms studied there were eight or more samples each of glioblastoma multiforme, meningioma and metastatic carcinoma. In the overall picture these tumors produced patterns which were

quite similar, but the pattern from specimen to specimen in a particular tumor was not constant. With this in mind, the validity of the results of the other tumors studied must be questioned, as in no case were there more than three samples of a particular category analyzed. Only the collection and analysis, with more refined techniques such as starch collum electrophoresis, of a large series of tumor specimen will answer this question.

SUMMARY

The results of the examination of 48 samples of tumor tissue, 18 samples of cyst fluid, 11 samples of serum and 5 samples of cerebrospinal fluid, from patients with lesions of the central nervous system, by means of paper strip electrophoresis are recorded. In addition, 11 samples of brain tissue, 8 samples of kidney tissue, 7 samples of spleen tissue and standard values of serum from humans are used as controls.

The tumor tissue, consisting of 16 cases of glioblastoma, 3 cases of astrocytoma, 8 cases of metastatic carcinoma, 11 cases of meningioma, 3 cases of acoustic neurinoma, 2 cases of oligodendroglioma, 2 cases of pituitary adenoma, 1 case of ependymoblastoma, 1 case of neurofibroma and 1 case of neuroblastoma are compared

with each other and with the protein values of the cyst fluid and normal brain tissue. Indications of a different protein composition of each of the tumors and between the tumors and normal brain were found.

The cyst fluids were taken from 4 cases of glioblastoma, 3 cases of astrocytoma, 2 cases of metastatic carcinoma, 2 cases of meningioma, 1 case of oligodendroglioma, 1 case of pituitary adenoma, 1 case of neurofibroma and 4 cases of craniopharyngioma. The protein values were compared with the values from normal and pathological serum, cerebrospinal fluid and tissue. In the pituitary adenoma cyst fluid, the protein values were similar to those of the tumor tissue, while in the remainder of the samples, the values were similar to those of normal serum.

The serum samples were taken from 4 cases of glioblastoma, 1 case of astrocytoma, 1 case of metastatic carcinoma, 1 case of meningioma, 1 case of oligodendroglioma, 1 case of pituitary adenoma, 1 case of neurofibroma and 1 case of craniopharyngioma. The protein values were compared with those of cyst fluid and normal serum. A hypoalbuminemia and an increase in some of the globulin fractions were generally found.

Cerebrospinal fluid from 2 cases of glioblastoma, 1 case of acoustic neurinoma, 1 case of craniopharyngioma and 1 case of

sarcoma were compared with normal serum protein values. In all cases a low albumin was found and in three out of five cases there was an increase in the beta globulin segment.

TABLE VI

NORMAL BRAIN TISSUE ELECTROPHORESIS

RESULTS IN PERCENT

CASE	ALBUMIN	ALPHA-1	ALPHA-2	BETA	GAMMA	
1	11.4	1.4	12.0	38.4	36.9	
3	1.0	4.8	8.0	51.3	34.9	grey matter
3	0.9	3.3	6.5	64.7	24.7	white matter
4	0.0	0.3	4.3	27.5	67.8	
5	0.0	2.5	13.2	27.7	56.6	cerebrum
5	0.0	0.0	9.8	37.7	52.5	cerebellum
6	2.2	5.8	9.4	39.6	43.2	
7	2.9	2.9	10.7	36.4	47.1	
8	3.3	3.3	10.0	33.3	50.0	
9	1.0	3.0	5.1	43.4	47.5	
10	0.0	0.0	15.2	24.2	60.6	
MEAN	2.1	2.5	9.5	38.6	47.4	
RANGE	11.4- 0.0	5.8- 0.0	15.2- 4.3	64.7- 24.2	67.8- 24.7	

FETAL BRAIN TISSUE

2	4.6	3.9	24.7	14.5	52.3	3 mo. pre.
11	3.6	12.2	18.2	34.3	31.7	6 wks. pre.

TABLE VII

NORMAL KIDNEY TISSUE ELECTROPHORESIS

RESULTS IN PERCENT

CASE	ALBUMIN	ALPHA-1	ALPHA-2	BETA	GAMMA
1	0.0	0.0	0.0	41.3	58.7
2	4.9	1.6	3.8	54.6	35.0
3	2.3	2.3	3.2	44.0	48.2
4	3.2	1.9	6.0	50.0	38.9
5	6.3	3.8	7.5	43.8	38.8
6	3.2	2.3	4.6	53.4	36.5
7	2.1	1.6	5.9	49.2	41.2
8	5.2	2.2	4.5	52.2	35.8
MEAN	3.4	2.0	4.4	48.6	41.6
RANGE	6.3-0.0	3.8-0.0	7.5-0.0	54.6-41.3	58.7-35.0

TABLE VIII

NORMAL SPLEEN TISSUE ELECTROPHORESIS

RESULTS IN PERCENT

CASE	ALBUMIN	ALPHA-1	ALPHA-2	BETA	GAMMA
1	0.0	0.0	0.0	80.5	19.5
2	0.5	0.7	2.1	82.8	13.5
3	1.1	3.2	6.4	64.0	25.2
4	4.1	1.1	3.2	74.3	17.2
5	1.0	0.5	0.8	89.4	8.3
6	3.1	0.9	1.9	73.8	20.2
7	0.0	1.5	3.8	75.4	19.2
MEAN	1.4	1.1	2.6	77.2	17.6
RANGE	4.1-0.0	3.2-0.0	6.4-0.0	89.4-64.0	25.2-8.3

TABLE IX

TUMOR TISSUE ELECTROPHORESIS

RESULTS IN PERCENT

CASE	ALBUMIN	ALPHA-1	ALPHA-2	BETA	GAMMA	
			GLIOBLASTOMA MULTIFORME			
16	9.8	2.7	3.6	61.2	22.8	
22	25.2	3.1	4.5	43.0	24.3	
27	5.3	3.7	13.9	21.1	56.0	
30	4.9	6.9	15.4	17.8	55.0	
37	7.8	4.8	10.8	34.7	41.9	
41	3.2	13.4	9.3	43.3	30.8	
47	0.0	0.0	7.0	23.8	69.2	
48	0.0	0.0	24.9	19.5	55.6	
49	0.0	0.0	7.5	22.5	70.1	
53	3.9	10.1	29.5	30.2	26.2	
56	16.6	4.7	14.1	37.2	27.3	1st op.
56	0.0	0.0	8.5	36.2	55.3	2nd op.
58	2.5	16.8	11.2	54.7	14.8	
60	5.3	3.8	18.5	40.1	32.2	
66	1.4	2.0	4.8	74.1	17.7	
71	0.0	0.0	10.9	54.5	34.5	
MEAN	5.4	4.5	12.2	38.4	39.6	
RANGE	25.2- 0.0	16.8- 0.0	29.5- 3.6	74.1 17.8	70.1- 14.8	
			ASTROCYTOMA			
21	10.7	10.3	11.0	36.3	31.8	
36	12.1	4.8	5.0	65.8	12.4	
39	2.2	10.4	18.2	22.6	46.5	
MEAN	8.3	8.5	11.4	41.6	30.2	
RANGE	12.1- 2.2	10.4- 4.8	18.2- 5.0	65.8- 22.6	46.5- 12.4	

TABLE IX CONTINUED

CASE	ALBUMIN	ALPHA-1	ALPHA-2	BETA	GAMMA	
			PITUITARY ADENOMA			
43	3.4	1.5	3.0	42.9	49.2	
65	0.0	0.0	0.0	73.3	26.7	
MEAN	1.7	0.8	1.5	58.1	38.0	
RANGE	3.4-	1.5-	3.0-	73.3-	49.2-	
	0.0	0.0	0.0	42.9	26.7	
			EPENDYMOBLASTOMA			
						(prealbumin)
61	7.6	4.0	16.6	39.0	31.5	1.3
			METASTATIC CARCINOMA			
23	3.6	20.2	15.4	18.9	42.1	
34	10.2	3.6	9.9	52.2	24.1	
40	1.2	1.7	1.7	77.5	17.9	
42	4.4	2.0	1.6	61.6	30.4	
44	16.3	3.0	16.1	29.8	34.7	
46	0.0	0.0	6.6	37.7	55.7	
67	7.0	7.0	12.7	42.3	31.0	
68	3.6	1.5	15.3	40.8	38.8	
MEAN	5.8	4.9	9.9	45.1	34.3	
RANGE	16.3-	20.0-	16.1-	77.5-	55.7-	
	0.0	0.0	1.6	18.9	17.9	
			MENINGIOMA			
25	27.0	6.2	13.2	15.3	38.4	
28	9.1	11.9	9.3	38.9	30.9	
31	10.0	5.0	12.2	23.9	48.9	
33	2.5	11.1	29.0	27.8	29.6	
45	4.4	2.6	7.0	44.7	41.2	1st sample
45	3.7	2.2	3.7	40.7	49.6	2nd sample
55	16.6	6.7	12.4	18.0	46.2	
57	8.7	2.7	14.8	28.2	45.6	

TABLE IX CONTINUED

CASE	ALBUMIN	ALPHA-1	ALPHA-2	BETA	GAMMA
MENINGIOMA					
59	7.5	3.7	8.6	57.8	22.4
63	0.0	0.0	7.1	57.9	35.1
72	0.0	3.3	9.8	54.3	32.6
MEAN	8.1	5.0	11.6	37.0	38.2
RANGE	27.0-0.0	11.9-0.0	29.0-3.7	57.9-15.3	49.6-22.4
ACOUSTIC NEURINOMA					
26	6.7	3.2	13.6	58.9	17.7
38	5.5	7.3	11.8	48.2	27.3
54	3.8	4.1	8.7	61.2	22.3
MEAN	5.3	4.9	11.4	56.1	22.4
RANGE	6.7-3.8	7.3-3.2	13.6-8.7	61.2-48.2	27.3-17.7
NEUROFIBROMA					
62	10.8	24.3	10.8	35.1	18.9
OLIGODENDROGLIOMA					
32	7.8	3.9	17.6	41.2	29.4
69	0.0	0.0	9.5	58.1	32.4
MEAN	3.9	2.0	13.6	49.7	30.9
RANGE	7.8-0.0	3.9-0.0	17.6-9.5	58.1-41.2	32.4-29.4
NEUROBLASTOMA					
64	0.0	0.0	13.0	56.5	30.4

TABLE X

CYST FLUID ELECTROPHORESIS

RESULTS IN PERCENT

CASE	ALBUMIN	ALPHA-1	ALPHA-2	BETA	GAMMA	
			GLIOBLASTOMA MULTIFORME			
7	37.7	6.1	20.8	14.3	21.3	
14	56.7	5.8	9.7	10.5	17.2	
17	40.5	7.6	14.1	16.5	21.3	
70	44.1	8.8	8.8	20.6	17.6	
MEAN	44.8	7.1	13.4	15.5	19.4	
RANGE	56.7- 37.7	8.8- 5.8	20.8- 8.8	20.6- 10.5	21.3- 17.2	
			ASTROCYTOMA			
8	56.3	4.2	7.4	11.8	20.4	
10	59.3	5.6	7.9	15.1	12.1	
36	48.6	6.4	9.1	22.4	13.4	
MEAN	54.7	5.4	8.1	16.4	15.3	
RANGE	59.3- 48.6	6.4- 4.2	9.1- 7.4	22.4- 11.8	20.4- 12.1	
			MENINGIOMA			
13	61.7	5.4	6.8	14.4	11.7	1st sample
13	61.7	5.4	4.2	14.5	13.3	2nd sample
MEAN	61.7	5.4	5.5	14.5	12.5	
RANGE	61.7	5.4	6.8- 4.2	14.5- 14.4	13.3- 11.7	

TABLE X CONTINUED

CASE	ALBUMIN	ALPHA-1	ALPHA-2	BETA	GAMMA
		METASTATIC CARCINOMA			
4	62.0	3.0	4.3	10.4	20.5
34	50.8	5.4	8.5	23.8	11.5
MEAN	56.4	4.2	6.4	17.1	16.0
RANGE	62.0-	5.4-	8.5-	23.8-	20.5-
	50.8	3.0	4.3	10.4	11.5
		OLIGODENDROGLIOMA			
12	64.3	5.1	4.6	12.6	14.4
		PITUITARY ADENOMA			
6	26.6	1.5	2.3	60.4	9.3
		NEUROFIBROMA			
1	42.3	10.2	9.0	19.3	21.6
		CRANIOPHARYNGIOMA			
2	49.9	4.1	10.5	22.5	13.1
5	65.9	3.5	5.5	14.0	11.2
11	52.9	3.7	4.1	11.2	28.4
35	42.1	2.6	5.6	24.6	25.1
MEAN	52.7	3.5	6.4	18.1	19.5
RANGE	65.9-	4.1-	10.5-	24.6-	28.4-
	42.1	2.6	4.1	11.2	11.2

TABLE XI

SERUM ELECTROPHORESIS

RESULTS IN PERCENT

CASE	ALBUMIN	ALPHA-1	ALPHA-2	BETA	GAMMA
GLIOBLASTOMA MULTIFORME					
14	56.5	5.1	10.7	10.5	17.4
56	37.2	11.0	20.6	17.4	13.8
66	37.2	10.7	15.9	18.4	17.8
70	42.4	10.3	10.0	23.2	14.1
MEAN	43.3	9.3	14.3	17.4	15.5
RANGE	56.5- 37.2	11.0- 5.1	20.6- 10.0	23.2- 10.5	17.8- 13.8
NEUROFIBROMA					
1	36.7	9.9	18.7	15.5	19.4
METASTATIC CARCINOMA					
4	51.9	3.7	3.7	28.4	12.5
PITUITARY ADENOMA					
6	59.6	3.4	9.1	15.9	12.2
CRANIOPHARYNGIOMA					
35	44.4	5.6	14.6	15.3	20.1
ASTROCYTOMA					
36	45.0	9.6	20.6	12.1	12.8
OLIGODENDROGLIOMA					
69	40.2	5.7	9.2	26.4	18.4
MENINGIOMA					
72	49.3	6.9	15.7	14.3	13.8

TABLE XII

CEREBROSPINAL FLUID ELECTROPHORESIS

RESULTS IN PERCENT

CASE	ALBUMIN	ALPHA-1	ALPHA-2	BETA	GAMMA
SARCOMA					
15	44.2	16.4	7.8	9.9	21.8
ACOUSTIC NEURINOMA					
26	46.2	5.7	7.5	20.4	20.2
CRANIOPHARYNGIOMA					
35	29.6	3.0	4.7	49.1	13.6
GLIOBLASTOMA MULTIFORME					
50	40.9	4.5	4.5	27.9	22.1
51	15.0	16.3	13.8	16.3	38.8

TABLE XIII

VARIATIONS OF TUMOR TISSUE FROM THE VALUES OF NORMAL BRAIN

NEOPLASM	ALBUMIN	ALPHA-1	ALPHA-2	BETA	GAMMA
Glioblastoma			+		-
Astrocytoma	+	+			--
Oligodendroglioma			+	+	--
Metastatic		+			-
Meningioma	+	+			-
Acoustic Neurinoma		+		++	--
Pituitary Adenoma		-	-	++	-
Ependymoblastoma	+		+		-
Neurofibroma	+	++			--
Neuroblastoma	-	-	+	++	--

CHART 1

NORMAL BRAIN TISSUE 11 CASES

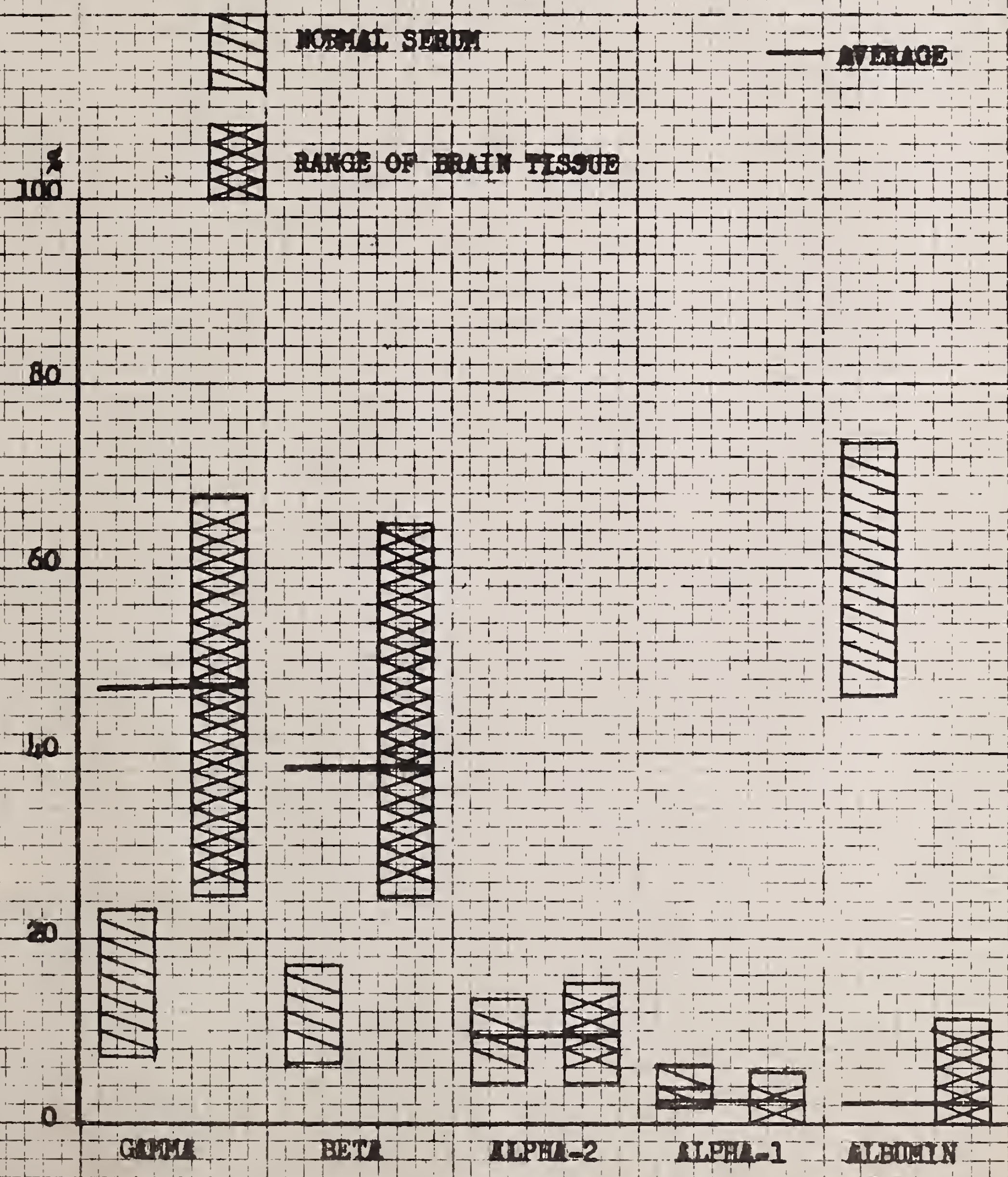


CHART 2

NORMAL KIDNEY TISSUE 8 CASES

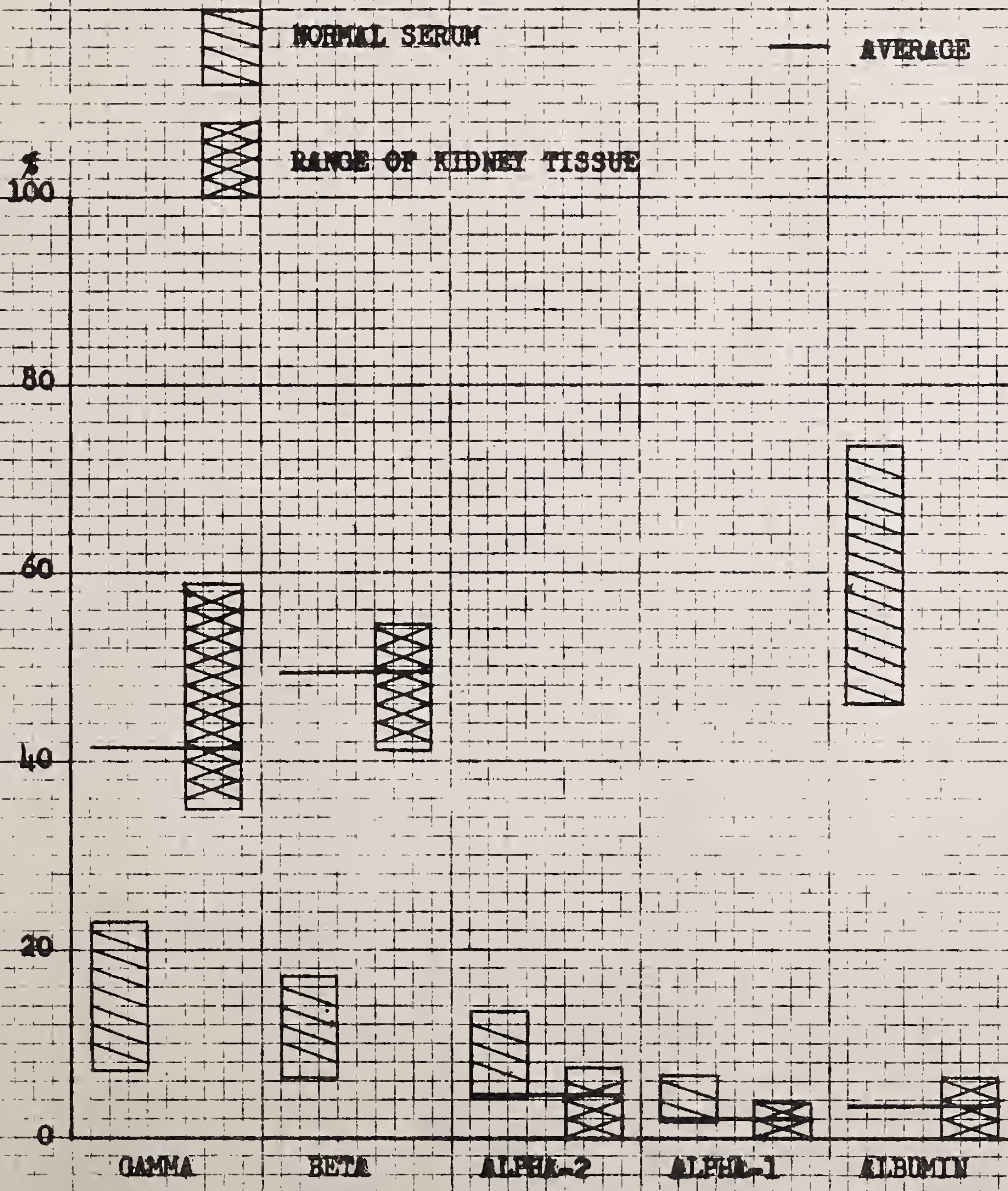
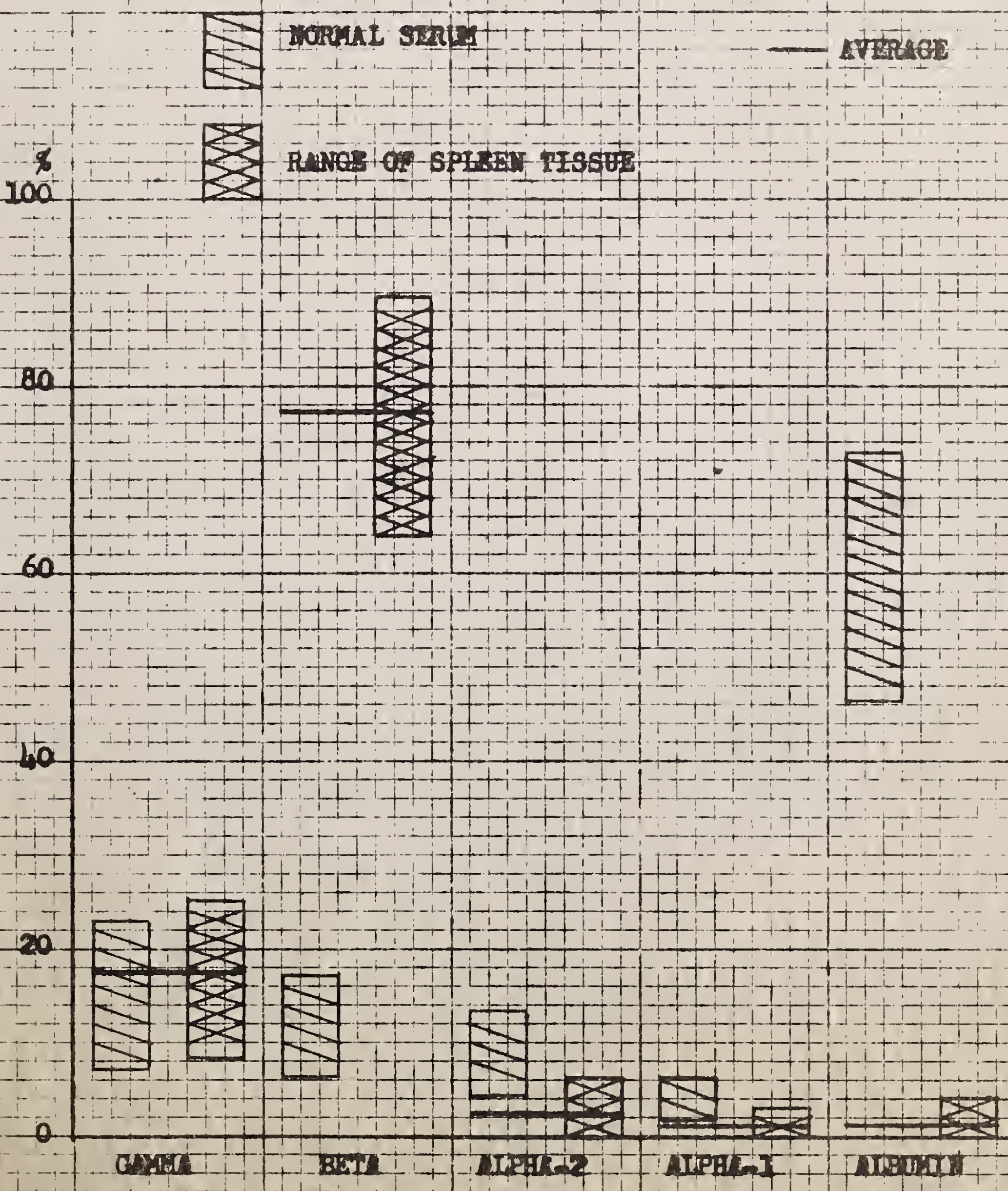


CHART 3

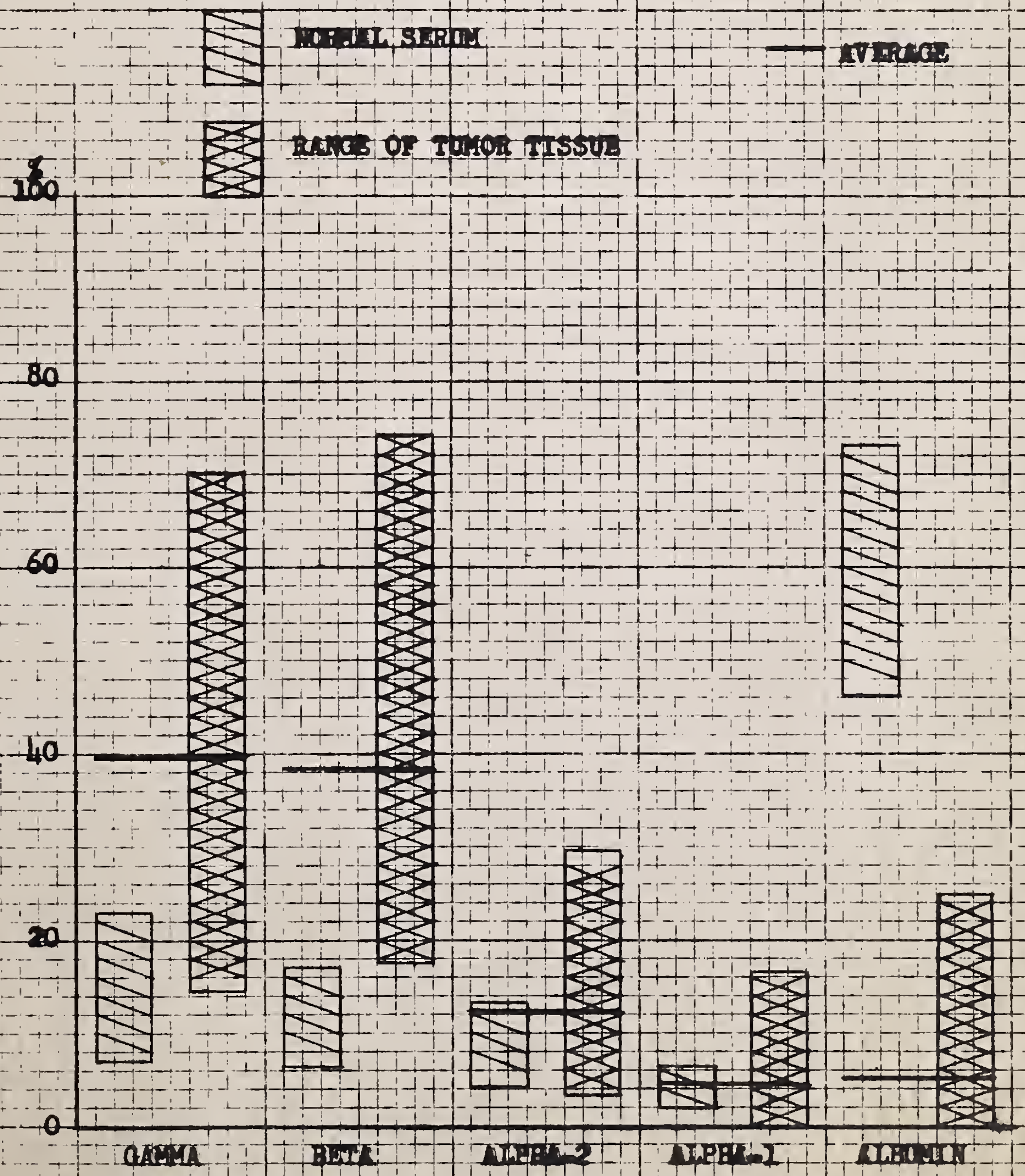
NORMAL SPLEEN TISSUE 7 CASES



Champion Filler No. 842-10 Squares to inch

CHART 4

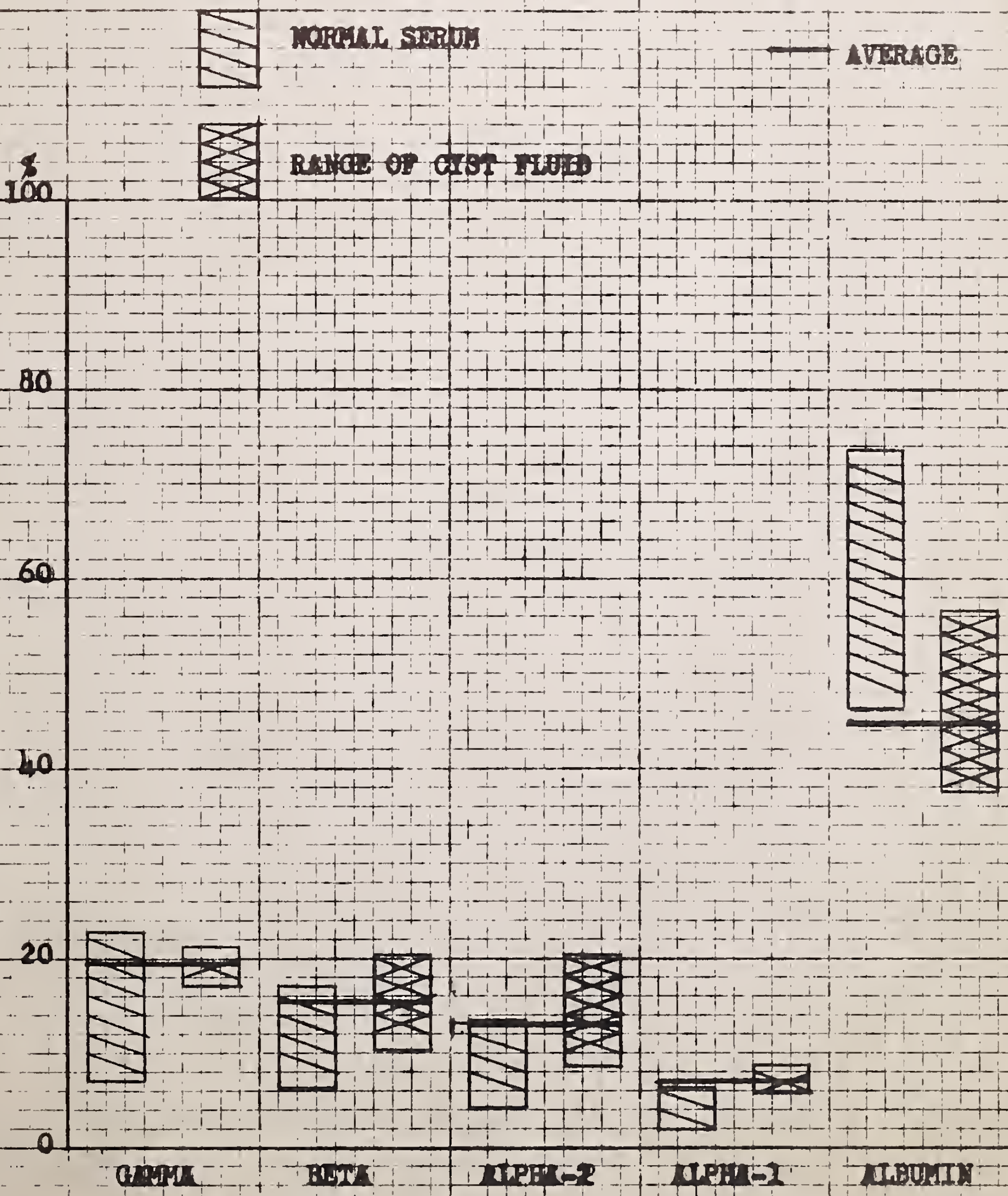
GLIOBLASTOMA MULTIFORME TUMOR TISSUE 16 CASES



Champion Filler No. 942—10 Squares to Inch

CHART 5

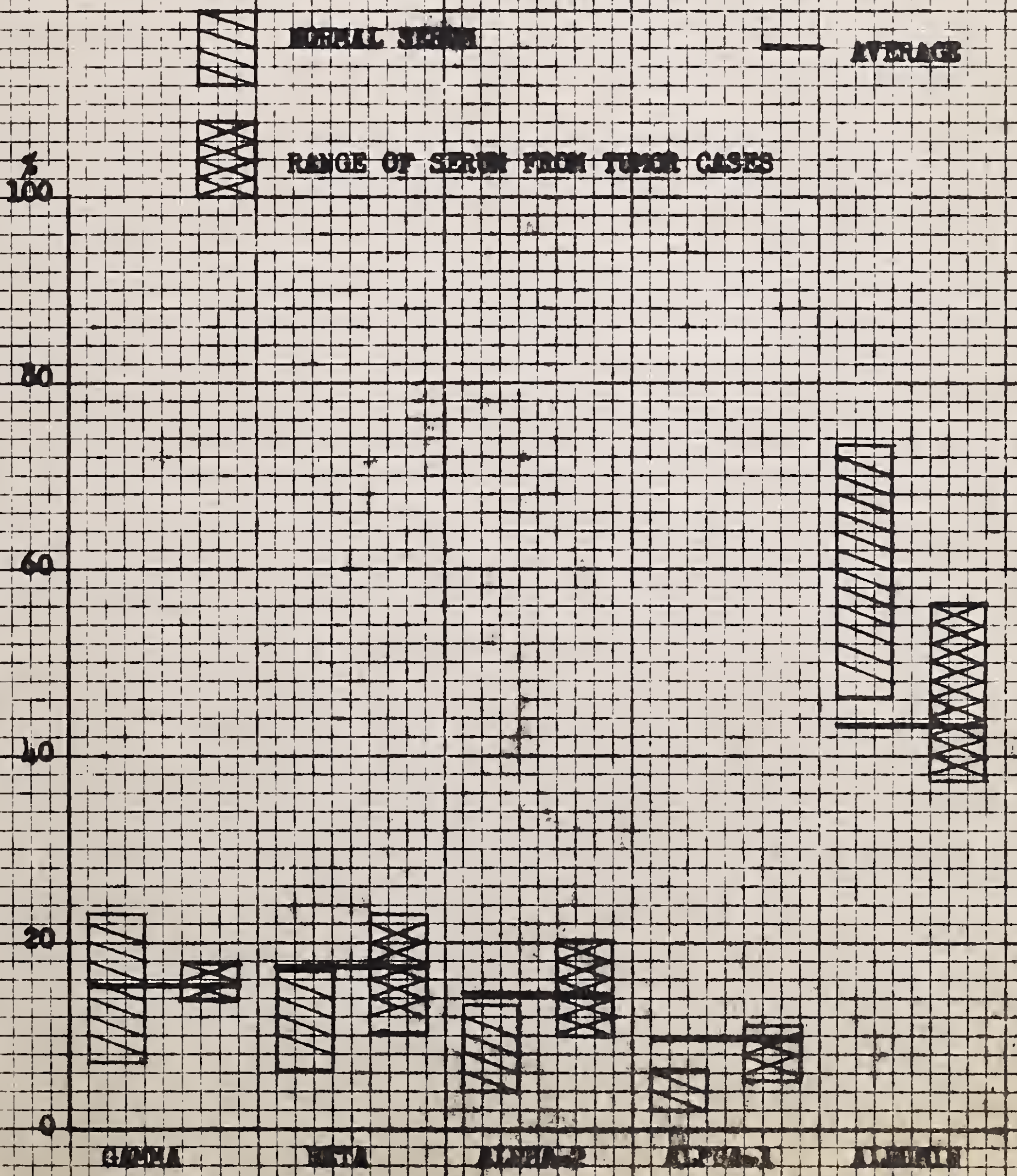
GLIOBLASTOMA MULTIFORME CYST FLUID 4 CASES



Champion Filler No. 642 10 Squares to Inch

CHART 6

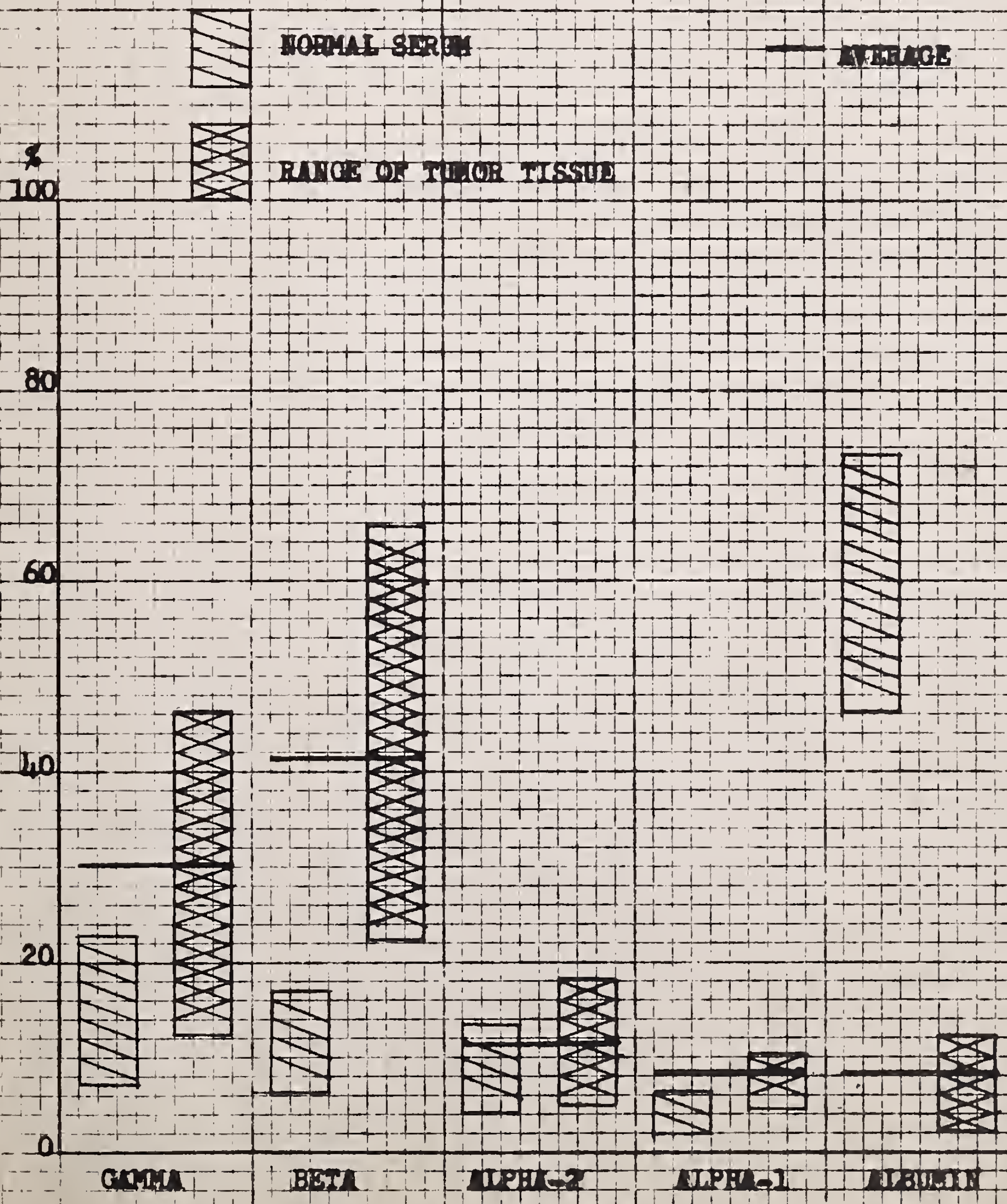
GLIOBLASTOMA MULTIFORME SERUM 4 CASES



Champion Filler No. 642-10 Squares to Inch

CHART 7

ASTROCYTOMA TUMOR TISSUE 3 CASES



Champion Filler No. 642-10 Squares to Inch

CHART 8

ASTROCYTOMA CYST FLUID 3 CASES

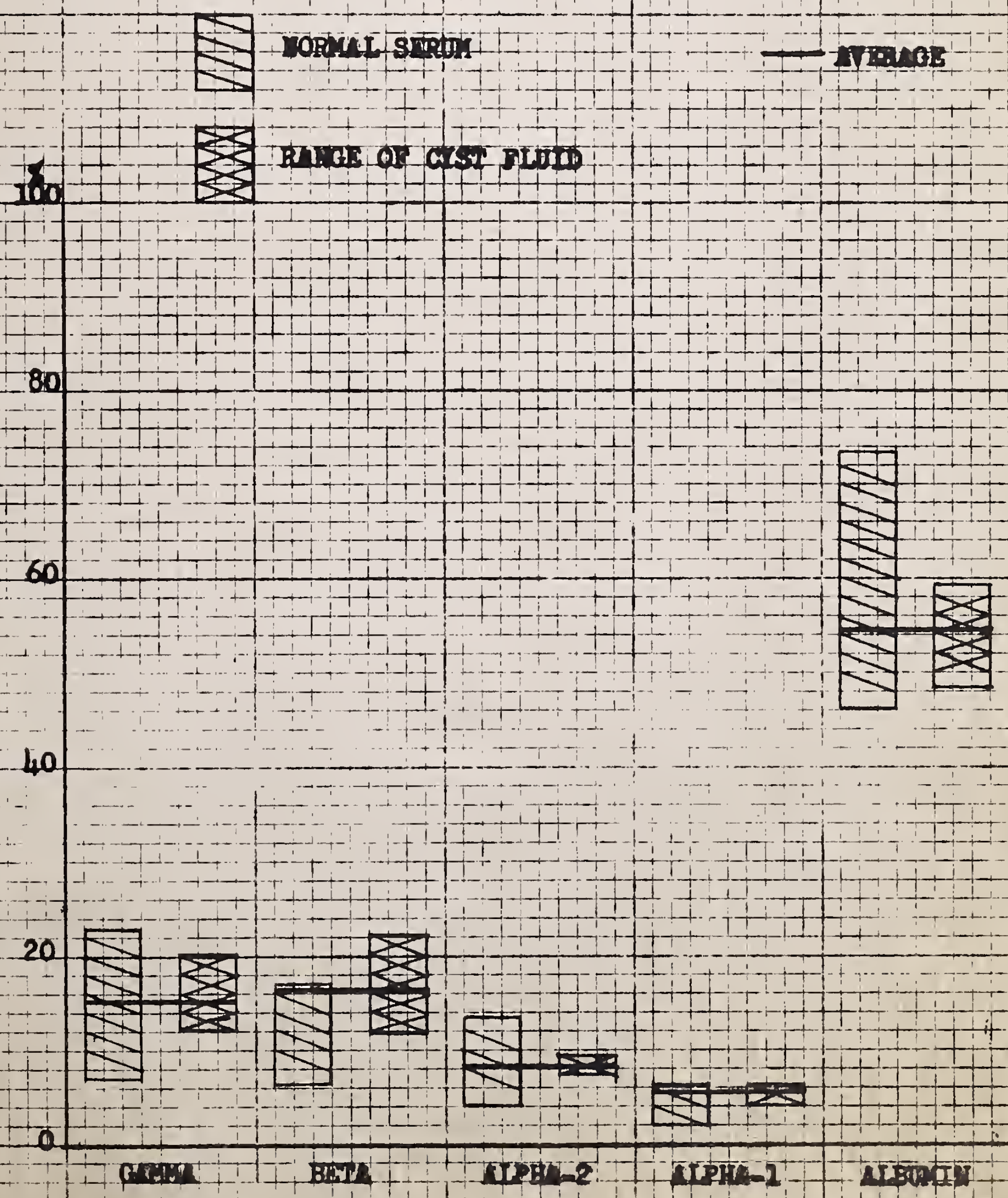
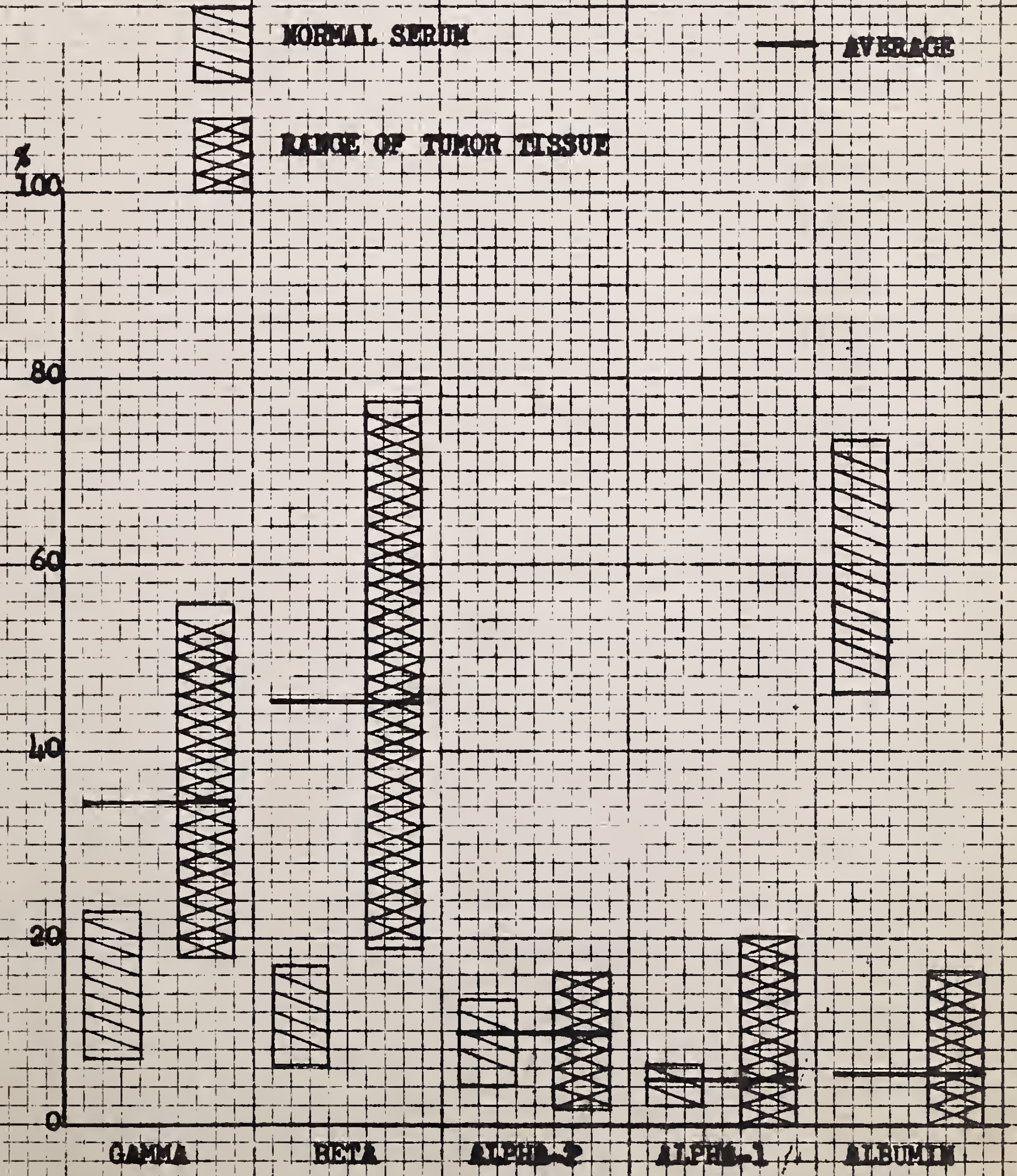


CHART 9

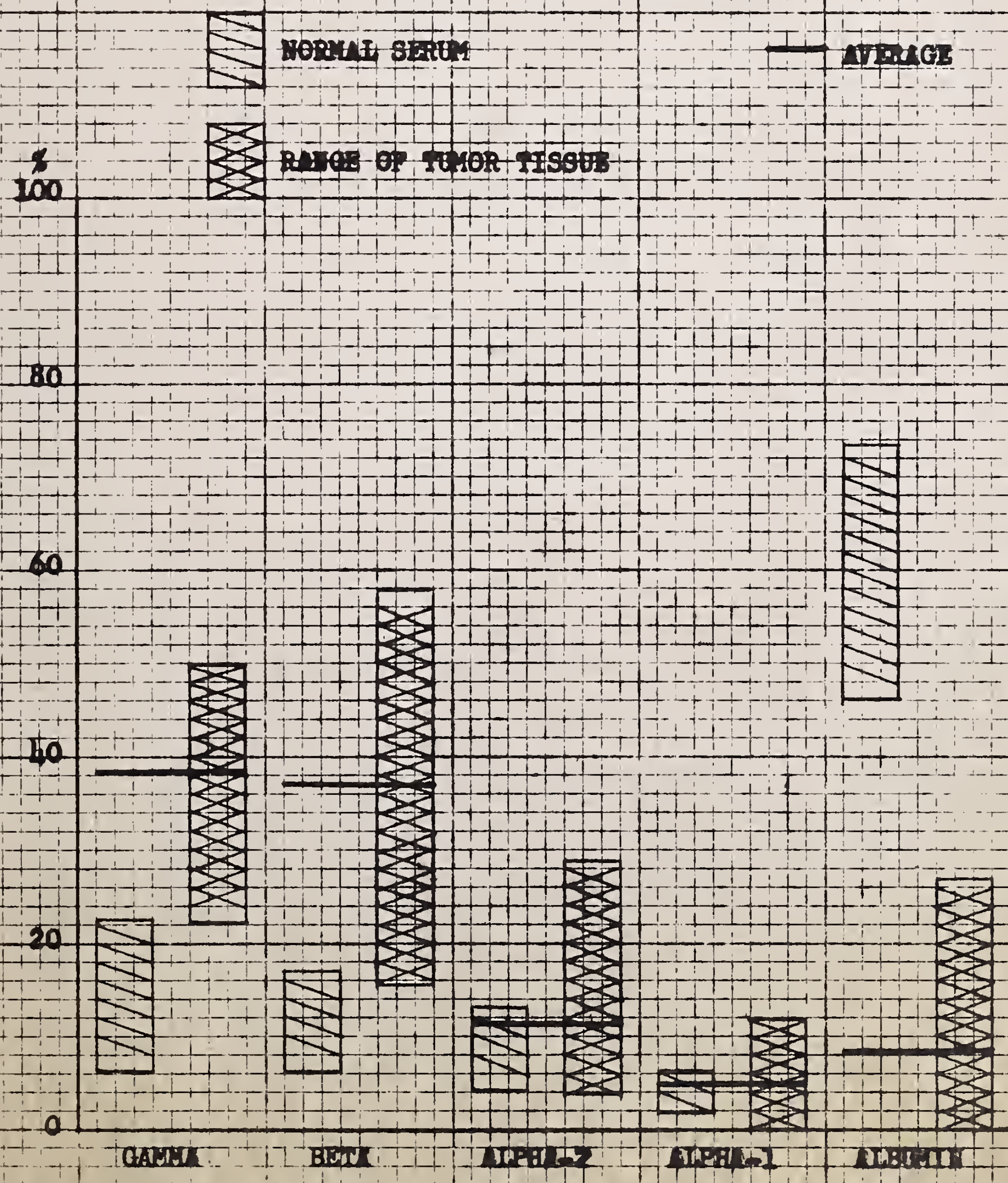
METASTATIC TUMORS TO THE BRAIN 8 CASES



Champion Filler No. 642—10 squares to inch

CHART 10

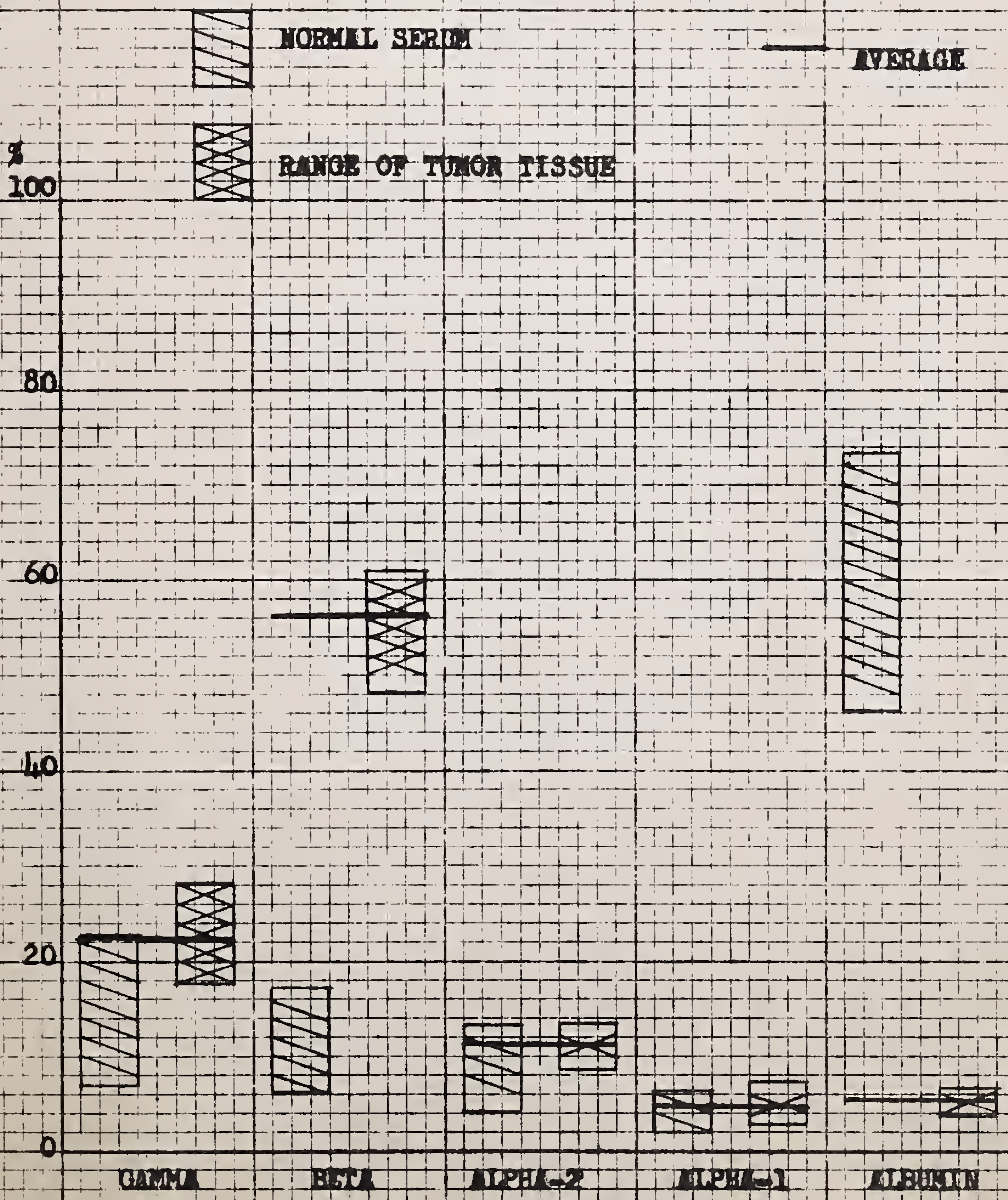
MENINGIOMA TUMOR TISSUE 11 CASES



Champion Filler No. 642--10 Squares to Inch

CHART 11

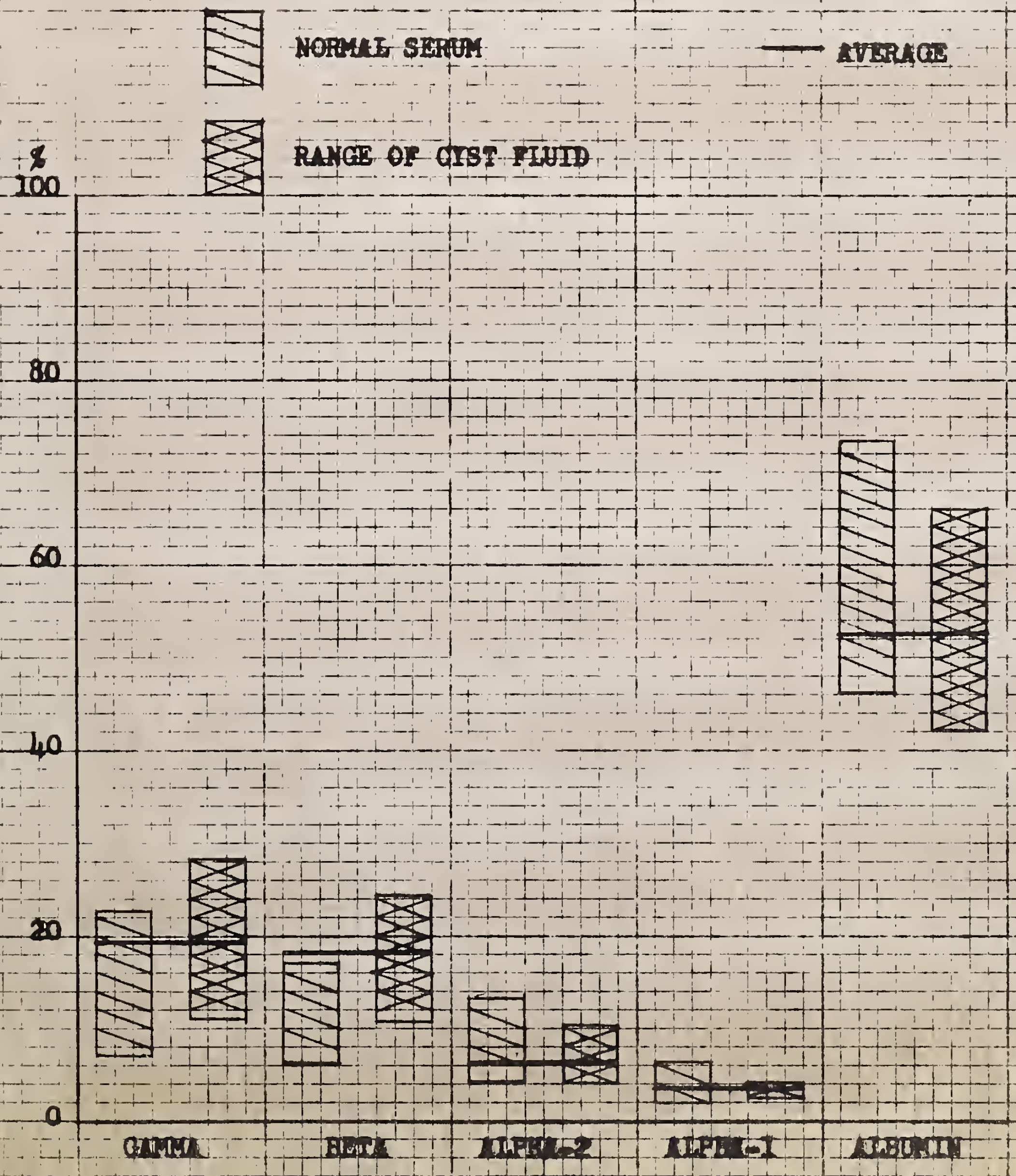
ACOUSTIC NEURINOMA TUMOR TISSUE 3 CASES



Champion Filler No. 642—10 Squares to Inch

CHART 12

CRANIOPHARYNGIOMA CYST FLUID 4 CASES



Champion Filler No. 642—10 Squares to Inch

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